

CLAIMS

- 2        1. A method for delivering a therapeutic dose of a gene expression  
cassette in a fluid selectively to heart for sustained expression comprising  
steps of:
  - 4            (a) increasing dwell time of fluid in a targeted area,
  - 6            (b) administration of a vascular permeabilizing agent, and
  - 8            (c) administration of a viral vector containing a gene expression  
cassette of interest.
- 10        2. A method as in claim 1, wherein the dwell time is increased by the  
induction of hypothermia.
- 12        3. A method as in claim 1, wherein the dwell time is increased by isolation  
of the heart from systemic circulation.
- 14        4. A method as in claim 1, wherein the dwell time is increased by  
induction of hypothermia and isolation of the heart from systemic circulation.
- 16        5. A method as in claim 1, wherein dwell time is increased by induction of  
complete or near-complete transient cardiac arrest.
- 18        6. A method as in claim 1, wherein dwell time is increased by induction of  
reversible bradycardia.
- 20        7. A method as in claim 1, wherein the vascular permeabilizing agent is  
histamine, substance P or serotonin.
- 22        8. A method as in claim 1, wherein at least one bolus of virus is  
administered.
- 24        9. A method as in claim 1, wherein the viral vector is an adenoviral vector.
- 26        30        10. A method as in claim 9, wherein the adenoviral vector contains a strong  
promoter.

2 11. A method as in claim 10, wherein the strong promoter is a  
cytomegalovirus (CMV) promoter.

4 12. A method as in claim 10, wherein the strong promoter is a Rous  
sarcoma virus (RSV) promoter.

6 13. A method as in claim 9, wherein the adenoviral vector contains  
8 enhancer elements.

10 14. A method as in claim 13, wherein the enhancer is a cytomegalovirus  
(CMV) enhancer.

12 15. A method as in claim 13, wherein the enhancer is a Rous sarcoma  
14 virus (RSV) enhancer.

16 16. A method as in claim 1, wherein the viral vector is an adenovirus-  
18 associated viral (AAV) vector.

20 17. A method as in claim 16, wherein the AAV vector contains a strong  
promoter.

22 18. A method as in claim 17, wherein the strong promoter is a  
cytomegalovirus (CMV) promoter.

24 19. A method as in claim 16, wherein the strong promoter is a Rous  
26 sarcoma virus (RSV) promoter.

28 20. A method as in claim 9, wherein the AAV vector contains enhancer  
30 elements.

32 21. A method as in claim 20, wherein the enhancer is a cytomegalovirus  
(CMV) enhancer.

34 22. A method as in claim 20, wherein the enhancer is a Rous sarcoma  
virus (RSV) enhancer.

2 23. A method as in claim 1, wherein the gene of interest is a structural  
gene.

4 24. A method as in claim 23, wherein the structural gene is  $\alpha$ -sarcoglycan.

6 25. A method as in claim 23, wherein the structural gene is  $\beta$ -sarcoglycan.

8 26. A method as in claim 23, wherein the structural gene is  $\gamma$ -sarcoglycan.

10 27. A method as in claim 23, wherein the structural gene is  $\delta$ -sarcoglycan.

12 28. A method as in claim 1, wherein the gene of interest is a functional  
gene.

14 29. A method as in claim 28, wherein the functional gene is  $\beta$ -adrenergic  
16 receptor ( $\beta$ -AR).

18 30. A method as in claim 28, wherein the functional gene is sarcoplasmic  
20 reticulum  $\text{Ca}^{2+}$  ATPase (SERCA-2).

22 31. A method as in claim 1, wherein the gene of interest is a gene  
fragment.

24 32. A method as in claim 1, wherein the gene of interest is a mutated form  
26 of a gene.

28 33. A method as in claim 32, wherein the mutated form of the gene is a  
dominant negative form of phospholamban (PLB).

30 34. A method as in claim 32, wherein the SERCA-2 gene is administered in  
32 conjunction with a dominant negative form of PLB.

34 35. A method as in claim 33, wherein the dominant negative form of PLB  
contains a mutation at amino acid 2 from glutamic acid (E) to alanine (A).

36. A method as in claim 33, wherein the dominant negative form of PLB contains a mutation at amino acid 14 from arginine (R) to glutamic acid (E).

37. A method as in claim 33, wherein the dominant negative form of PLB contains a mutation at amino acid 16 from serine (S) to asparagine (N).

38. A method as in claim 33, wherein the dominant negative form of PLB1 contains mutations at amino acid 16 from serine (S) to glutamic acid (E).

39. A method as in claim 33, wherein the dominant negative form of PLB contains a mutation at amino acid 49 from valine (V) to alanine (A).

40. A method as in claim 33, wherein the dominant negative form of PLB contains mutations at amino acid 3 from lysine (K) to glutamic acid (E) and at amino acid 14 from arginine (R) to glutamic acid (E).